

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Patent Application of)
Ju-Ock NAM et al.) Group Art Unit: 1654
Application No.: 10/552,291) Examiner: Christina Bradley
Filed: October 3, 2005) Confirmation No.: 6194
For: USE OF A PEPTIDE THAT)
INTERACTS WITH ALPHA V BETA)
3 INTEGRIN OF ENDOTHELIAL)
CELL)

DECLARATION OF DR. In San Kim

Commissioner for Patents
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Alexandria, VA 22313-1450

Sir:

1. I, Dr. In-San Kim, declare the following:
2. I am a citizen of the Republic of Korea, and have the following mailing address: Cell and Matrix Research Institute; Department of Biochemistry and Cell Biology, Kyungpook National University School of Medicine, 101 Dongin-Dong, Jung-gu, Daegu, 700-422, Republic of Korea;
3. I graduated from Kyungpook National University School of Medicine with M.D. and a Ph.D. degrees in 1989;
4. I am a professor in the Department of Biochemistry and cell Biology of Kyungpook National University School of Medicine;
5. I have read and am familiar with the above-identified United States patent application filed October 3, 2004, and I am submitting this Declaration in support of that application;
6. I have performed and/or supervised the experiments reported below:

In order to examine whether β ig-h3 comprising peptide of the present invention (YH18) has anti-tumor activity, the inventors of the above-identified application were performed the following example.

Example : Analysis of anticancer effect of βig-h3

The amino acid sequence of βig-h3 is as follow:

βig-h3 comprising peptide of the present invention (SEQ ID NO.: 1 of the present invention)

MALFVRLLAGPAATLAGPAKSPYQLVLQHSRLRGRQHGPNV
CAVQKVIGTNRKYFTNCKQWYQRKICGKSTVISYECCPGYEKVPGEK
GCPAALPLSNLYETLGVVGSTTTQLYTDRTEKLPEMEGPGSFTIFAP
SNEAWASLPAEVLDLSLVSNVNIELLNALRYHMVGRRLTDELKGMLT
TSMYQNSNIQIHYPNGIVTVNCARLLKADHHATNGVVHLIDKVISTIT
NNIQQIIEIEDTFETLRAAVAASGLNTMLENGNGQYTLLAPTNNEAFEKIP
SETLNRLGDPEALRDLLNNHILKSAMCAEAIVAGLSVETLEGTTLEVG
CSGDMLTINGKAIISNKDILATNGVIHYIDELLIPDSAKTLFELAAESDV
STAIDLFRQAGLGNHLGSERLTLLAPLNSVFKDGTTPPIDAHTRNLLR
NHIIKDQLASKYLYHGQTLETLGKGLRVFVRNSLCIENSCIAAHDKR
GRYGTFLTMDRVLTTPMGTVMVDVLKGDNRFSLVAAIQSAGLTETLN
REGVYTVFAPTNEAFRALPPRERSRLLGDAKELANILKYHIGDEILVS
GGIGALVRLKSLQGDKLEVSLKNNVVSVNKEPVAEPDIMATNGVVHVI
TNVLQPPANRPQERGDELADSALEIFKQASAFSRASQRSVRLAPVYQ
KLLERMKH

The shaded and underlined amino acid sequences are included in the sequence listing of the invention.

1-1: Test of tumor growth inhibitory effect of βig-h3

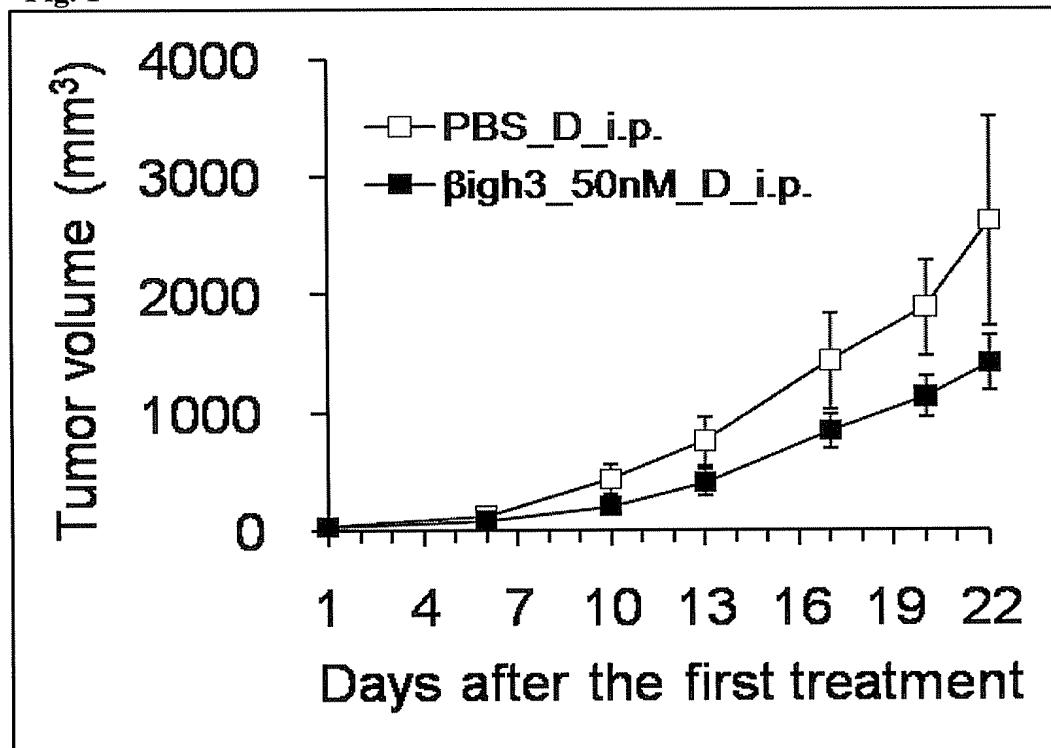
To confirm the inhibitory effect of βig-h3 against tumor growth, the present inventors performed a test using BALB/c nude mice.

LLC cells(mouse Lewis lung carcinoma) were suspended in culture medium at a density 1×10^6 cells/ml. 0.1ml of the cell suspension was injected to the flank subcutis of 5-6 week-old male BALB/c nude mouse(purchased from Jung-Ang Animal Inc. Ltd., Korea) to make a subcutaneous tumor model. The mice were divided into two groups, the control group and the test group and each group consisted of five mice. The mice of test group were i.p. injected daily with the indicated recombinant proteins in a total volume of 0.1 ml PBS. The mice of the control group were given an equal volume of PBS each day. The tumor sizes of the control group were measured using Vernier calipers every 2 to 4 days, and the volumes were calculated using the standard formula: width² × length × 0.52.

The result showed that, as shown in FIG. 1, the tumor in the control group started to grow rapidly from 10th day after tumor induction. On the other hand, the tumor in the experimental group showed gentle growth curve compared to that of the

control group. The above test shows that the growth rate with time of the test group was lower than that of the control group. In conclusion, it shows β ig-h3 has inhibitory effect on tumor growth.

<Fig. 1>



7. The results detailed above demonstrate that a peptide according to the present invention can be used to treat cancer in a well-accepted lung cancer animal model;

8. I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patent issued thereon.

Date: Jan. 20. 2009

By: In San Kim
In San Kim